

REMARKS

Reexamination and reconsideration are respectfully requested in view of the foregoing amendments and the following remarks. The amendments thus are without disclaimer and without prejudice to Applicant's rights to pursue any canceled subject matter in this application or in a continuing application.

1. Status of the Claims

The status of the claims following entry of the amendment is as follows:

Claims canceled: Claims 1 and 22-32

Claims added: Claims 33-36

Claims pending: Claims 2-21 and 33-36

Claims allowed: None

Claims rejected: Claims 1-32

Claims withdrawn: None

2. Support for the Amendments

Claims 2-6, 12, 13, 15, and 18-21 are amended to change claim dependency, clarify the nature of the claimed subject matter, and/or clarify antecedent basis. The amendment from "essentially purified" to "purified" in claim 12 and new claim 33 is supported, for example, at page 10, lines 12-14, of the specification. The amendments thus are without disclaimer and without prejudice to Applicant's rights to pursue any canceled subject matter in this application or in a continuing application.

New claims 33-36 are supported throughout the specification. A method of concentrating an active, glycosylated Dkk protein is supported by original claim 1 and in the specification at page 24, line 7, through page 25, line 19, for example. Concentrating a culture media containing an active, glycosylated Dkk protein is supported, for example, at page 17, line 7, though page 18, line 2, and by Examples 1 and 2, among other places. Concentrating in the presence of EDTA and a detergent to obtain a concentrated Dkk protein is supported at least at page 17, line 22, through page 18, line 2, and at page 18, lines 11-15. Support for a detergent that does not inhibit

the activity of the Dkk protein is found at least at page 18, line 15. Support for mammalian host cells expressing the Dkk protein and secreting the Dkk protein into the culture media is found throughout the specification, including page 11, lines 21-24 (defining “mammalian host cells”) and 13, line 31, *et seq.*

3. Request for Clarification Regarding Information Disclosure Statement

Applicants appreciate partial acknowledgment of the Information Disclosure Statement provided September 15, 2006; however, Applicants request an explanation for the failure to consider the references WO 99/46281, WO 98/46755, and WO 02/066509 with the Office’s next communication.

4. Rejection of the Claims Under 35 U.S.C. § 103(a)

Claims 1-32 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 7,446,181 B2 (“McCarthy”). Applicants traverse the rejection as it applies to the present claims.

McCarthy teaches secretion and post-translational modification (e.g., glycosylation) of a human Dkk protein from a 293T cell. McCarthy, col. 80, line 40, through col. 81, line 60. McCarthy teaches further large-scale purification of the Dkk protein. McCarthy, col. 81, line 61, through col. 82, line 27. In this procedure, McCarthy harvests conditioned medium containing an expressed and secreted Dkk protein. The conditioned medium is filtered and centrifuged, then purified under an anti-FLAG M2 affinity column in the presence of PBS and glycine. Eluted fractions containing the Dkk protein are analyzed by absorbance at 280 nm, Coomassie staining, silver staining and western blotting. *Id.*

McCarthy does not teach or suggest at least the claim elements of concentrating a culture media containing an active, glycosylated Dkk protein *in the presence* of EDTA and a detergent to obtain a concentrated Dkk protein, wherein the detergent does not inhibit the activity of the Dkk protein, as claimed. The Office alleges that McCarthy’s use of detergents disclosed at col. 54, lines 31-47, would have suggested the use of detergents during concentration of a culture media containing an active, glycosylated Dkk protein. The Office further alleges that the use of EDTA was well known in the art, and thus would have been *prima facie* obvious.

Whether a claim is obvious is based on an objective analysis of the scope and content of the prior art, the differences between the prior art and each element of the claimed invention, the level of skill in the pertinent art, and secondary considerations supporting a conclusion of non-obviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 15-17 (1966). “[O]bviousness requires a suggestion of all limitations in a claim.” *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985, 180 USPQ 580, 583 (CCPA 1974)).

In the present case, McCarthy’s process of producing a Dkk protein does not provide a concentrating step, and the Office produces no evidence that it would have been obvious to include one. *Compare* McCarthy, col. 81, line 61, through col. 82, line 27. So the Office has not made a case that all the elements of the claimed invention would have been obvious. The rejection is unsubstantiated for this reason. *See CFMT*, 349 F.3d at 1342. It must, therefore, be withdrawn.

Further, even if the Office could provide relevant evidence suggesting a concentration step, McCarthy’s process of producing a Dkk protein does not involve using a detergent and EDTA (*compare* McCarthy, col. 81, line 61, through col. 82, line 27), so there would have been no suggestion to use either in a concentrating step. McCarthy suggests using a detergent for the separate purpose of solubilizing Dkk in cell free assays. *See* McCarthy, col. 54, lines 31-47. The Office provides no reason, however, why solubilizing Dkk in cell free assays would have suggested the use of a detergent during concentration of Dkk. For this reason, too, the rejection is unsubstantiated and must be withdrawn. *See CFMT*, 349 F.3d at 1342.

Finally, the present disclosure provides secondary evidence that must be weighed in a consideration of obviousness. *See Graham*, 383 U.S. at 15-17; *see also In re Meinhardt*, 157 USPQ 270, 274-75 (CCPA 1968). Specifically, the specification teaches that the combination of EDTA and a detergent synergistically increases the overall yield of Dkk 5-fold, compared to the yield obtained with either alone:

The presence of Tween-20 (or other comparable detergents) and EDTA is necessary for better yields. In the absence of Tween-20 and EDTA, the yield of Dkk1 is low (less than about 1 mg of protein per liter of media). When Tween-20 or EDTA are *used separately*, a minor (i.e., about **1.2 to about 1.5 fold**) increase in yield is observed. However, when EDTA and Tween-20 are *combined*, these

reagents work synergistically to increase the overall yield *5-fold* as compared to their absence, whereby about 5 mg or more of Dkk1 is obtained per liter of media following over-expression and purification.

Specification, page 17, lines 22-29 (emphasis added); *see also* page 17, lines 30-34 (same with another detergent). Because of these secondary considerations, the claims are non-obvious, even if the Office *arguendo* established *prima facie* obviousness.


CONCLUSION

In conclusion, the application is believed to be in condition for allowance, and Applicants respectfully request indication of the same. Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience. This paper may be used as a constructive petition for an extension of time. If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0573.

Respectfully Submitted,

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By: _____



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